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(74) Agent: BOULT WADE TENNANT; Verulam Gardens,
70 Gray's Inn Road, London WC1X 8BT (GB).

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(71) Applicant (for all designated States except US): BIO-
QUELL MEDICAL LIMITED [GB/GB]; 30-31 Lynx
Crescent, Weston-Super-Mare, Somerset BS24 9BP (GB).

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(72) Inventors; and

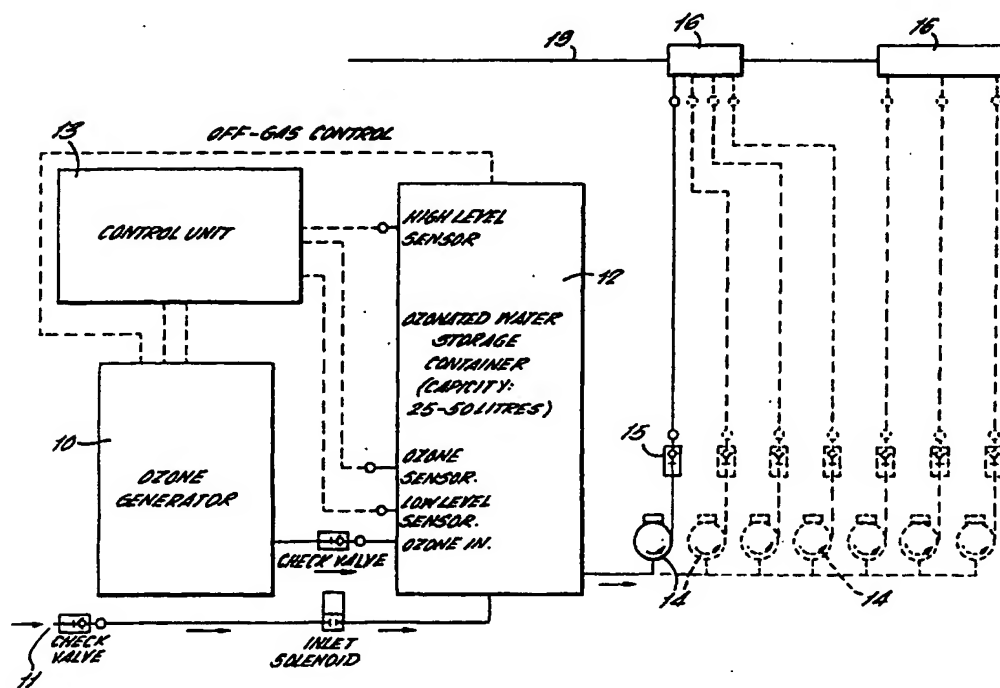
(75) Inventors/Applicants (for US only): DAINTREE, An-
drew [GB/GB]; The Withies, Rectory Lane, Lymphsam
BS24 0EN (GB). CURTIS, Beverley [GB/GB]; 27 Church
Close, Stoke St. Gregory, Taunton TA3 6HA (GB).

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(54) Title: MEDICAL DEVICE DISINFECTION



(57) Abstract: The disclosure relates to a method of disinfecting medical theatre care equipment comprising the steps of causing ozonated water to flow over the surfaces of the equipment at a predetermined concentration and flow rate for a predetermined time and monitoring the concentration of ozone in the water leaving the equipment. The flow is terminated when the concentration of ozone leaving the equipment is substantially the same as that being delivered to the equipment.

WO 01/58500 A1



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MEDICAL DEVICE DISINFECTION

5 This invention relates to the disinfection of
medical equipment such as endoscopes and other health
care equipment such as bed pans.

10 Medical devices and in particular endoscopes have
historically been disinfected by either heat or
chemicals. Current disinfection of endoscopes is
carried out by two methods; one a cold process, and
the other a heated process.

i) **Cold Process**

15 This is normally used when the endoscopes
cannot be disinfected by using heat, i.e.
most flexible endoscopes. The endoscopes
are manually cleaned and then put into a
washer disinfector for an automatic process.
20 This process gives the scopes a pre-wash, a
wash with a disinfectant, and a final rinse
with water. The disinfectant wash allows a
contact time dependent on the manufacturer
of the disinfectant, e.g. Cidex (Johnson and
Johnson), Nu-Cidex (Johnson and Johnson),
25 Gigasept (Schule and Mayer).

General
method

30 Cold processing allows a batch of
disinfectant to be re-used, the number of
cycles dependent on the washer disinfector
and the level of dilution taking place.
Once this number of cycles is completed, the
batch of disinfectant is dumped to waste and
the machine re-charged with a fresh batch.

35 ii) **Hot Process**

Some endoscopes (mainly rigid ones) can be

processed in a normal sterilising autoclave
at 120-130°C. For endoscopes such as
flexible ones that cannot withstand this
temperature, there are a range of washer
5 disinfectors that disinfect by heating to a
lower temperature of 50-55°C.

This process gives the scopes a pre-wash, a
heated wash with a small amount of
10 disinfectant, and then a final rinse with
water. The heated wash takes a small amount
of concentrated disinfectant, and by heating
to 50-55°C causes the chemical to vaporise
and thus provide the efficiency required.
15 This process normally uses gluteraldehyde as
the disinfectant, and the small amount used
each time is a single use. This process
tends to have longer cycle times than cold
processing.

20 The heated process is more prevalent in
Europe, while cold processing is utilised in
the UK and US.

25 The method of the invention also provides an
alternative to the use of steam.

Ozonated water is widely used to kill bacteria.
However, when generating and dissolving ozone in water
30 it is usual to expect levels of under 1 ppm. We have
found that we are not able to disinfect medical
devices to the required standard or within an
acceptable time period using such levels of ozone
concentration. Effective disinfection can only be
35 achieved with a precise combination of flow over and
through the device, ozone levels, and time.

The criteria for disinfection of the endoscopes have been developed by Dr. J Babb of the Hospital Infection Research Laboratory (HIRL) at City Hospital NHS Trust, Birmingham, as described later and is key to the validation of the process. The process fulfils the HIRL test criteria for endoscope washer disinfectors, i.e. mean \log_{10} reduction >6 (99.9999%) with no individual reduction <5 (see Appendix 3). Although external validation of the process can be undertaken, it is impractical to undertake on a daily basis. Within the process we have been able to measure the ozone levels at the inlet and outlet of the process. This has allowed us to calculate how long the process needs to run to give the required disinfection. As ozone concentration is depleted on contact with bacteria, if the inlet and outlet levels are identical there is minimal bacteria remaining. As bacteria levels have to be very low to validate the unit for a predetermined time after equilibrium is reached.

✓ Thus this invention relates to ozonated water as a substitute for the traditional chemical method of disinfection. Although the development and validation has been undertaken on endoscopes, the process and technology is relevant to many medical devices.

The invention provides a method of disinfecting medical equipment comprising the steps of causing ozonated water to flow over the surfaces of the equipment at a predetermined concentration and flow rate for a predetermined time and monitoring the concentration of ozone in the water leaving the equipment and terminating the flow when the concentration of ozone leaving the equipment is substantially the same as that being delivered to the equipment. Thus the rinse water produced does not

contain active sanitants.

The following is a description of some specific
embodiments of the invention, reference being made to
5 the accompanying drawings, in which:

Figure 1 is a schematic diagram showing the
apparatus used for carrying the disinfection of
medical equipment such as endoscopes; and

10

Figure 2 shows a number of different scopes to
which the cleaning process is applicable.

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Figure 1 shows a unit based around an
electrochemical generator stack 10, where Hydrogen (H)
and Ozone (O^3) are generated. The stack is fed by a
dedicated de-ionised water supply 11 at a pressure of
one bar, to maintain the integrity and efficiency of
the cells and the long-term quality of the feed water.
20 Power for the stack is supplied from a variable DC
supply (not shown). There is also a battery back-up
system (not shown) to support the cell in the event of
a power failure.

25

Hydrogen gas is re-absorbed and/or catalytically
converted. Ozone is supplied under pressure to a
contactor 12 containing 25-50 litres of filtered water
via a diffuser block. This allows the ozone gas to
bubble into the water to produce a high concentration
30 solution (typically at least 4 ppm, for example
6+ppm). The level of water in the contactor is
controlled and filled through solenoid valves, the
operations being initiated by a micro-processor
operated control unit 13 through software
35 instructions. Ozone concentration levels are
constantly monitored to ensure correct values.

Any excess ozone off-gas is collected at the top of the contactor and passed to a destruct column, where it is processed through an absorber. When operating at full capacity the cell produces perceptible heat, and so water used in the cell for electrolysing is cooled with a heat exchanger and refrigeration plant.

To disinfect effectively an endoscope, ozonated water needs to be pumped through all the internal channels of the scope at a flow rate and concentration level sufficient to kill organisms that may remain after a manual clean has taken place. The water is supplied at ambient temperature but could be pre-heated up to 40°C to accelerate the disinfection process if required. In our testing we have found these to be concentration level of at least 4ppm, preferably about 6ppm and not more than 15ppm, and a flow rate that equates to 2.2 L/min. These parameters need to be applied for a minimum period of 10 minutes and a maximum of 15 minutes to ensure all internal channels of a normal endoscope have been disinfected.

Time

Ozonated water is supplied from the contactor to a supply pump 14 having connectors 15 for coupling to the individual endoscope channels 16. Spent ozonated water is directed to waste via the distal end of the endoscope 19.

During testing and development a method was devised that determined whether ozone has achieved the intended uses. With a known concentration of ozonated water entering a test sample contaminated with "Pseudomonas aeruginosa NCTC 6749" of a known value, a second sensor was used to monitor the water output from the test equipment. When the exit concentration level rose to match the known input, it was assumed

that by then ozone had killed any remaining organisms. The flow of ozonated water was continued for a further 5 minutes after that equilibrium was reached. Sterile water samples were taken and cultured to established protocols and showed that the method had achieved the necessary kill rates, to be declared a process disinfectant.

Previous tests were conducted that used ozone concentrations that varied from 0.1-18ppm, and flow rates as low as 400ml/min. Contact times also varied from 5 minutes to as much as 25 minutes, but in all cases the kill rates achieved were inferior to those reached when the optimised settings previously stated were used.

KEY POINTS

- * Safe operating media - chemical disinfectants are sensitising agents and are possibly tetragenic.
- * Cold Process.
- * One Shot Process.
- * Process validated.
- * Closed loop system - ozone levels monitored at discharge.
- * Critical parameters of ozone concentration, flow discharge rates, and time established.
- * Residue free disinfectant.

TEST METHOD

The biopsy and suction channels of an Olympus gastroscope 20 (Type GIF Q10) shown in Figure 2 were contaminated having removed the air/water and suction valves 21,22 with an overnight broth culture of *Ps*.

aeruginosa NCTC 6749 enriched with 10% horse serum. The instrument was left to drain / dry for 10 minutes at room temperature before sampling, i.e. pre-disinfection count or processing and sampling, ie. post-disinfection count. The endoscope was re-contaminated prior to each test cycle. After processing in an endoscope washer disinfector by coupling supply and return conduits to the air/water and section valve parts, the endoscope channels were sampled to detect surviving test bacteria. This was done by flushing 10 ml of sterile water through the channel lumens and collecting the washings in a sterile container at the distal tip. These were diluted and plated onto typtone soya agar plates, which were incubated at 37°C for 18 hours. The number of colony forming units of the test organism were enumerated and counts transposed to the log₁₀ system. The log reduction (RF) were calculated for each cycle, i.e.:

$$\begin{aligned} \text{Log}_{10} \text{ pre-disinfection count} - \text{log}_{10} \text{ post-disinfection count} \\ = \text{log}_{10} \text{ reduction (RF)} \end{aligned}$$

It is normal to use a pre-disinfection count of 8 log₁₀ contamination and aim for a post-disinfection count of less than 2 log₁₀, giving a log₁₀ reduction of 6.

Similar methods are used for colonoscopes (see Figure 3) and duadenoscopes (see Figure 4).

Definition of Disinfection

PHLS - Chemical Disinfection in Hospitals

Definitions

Disinfection: A process used to reduce the number of micro-organisms but not usually of bacterial spores; the process does not necessarily kill or remove all micro-organisms, but reduces their number of a level which is not harmful to health. The term is applicable to the treatment of inanimate objects and materials and may also be applied to the treatment of the skin, mucous membranes and other body tissues and cavities.

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ENDOSCOPE TESTS

Log₁₀ reductions in test bacteria from the biopsy and suction channels of two endoscopes using ozonated water for 10 minutes

Contact time	Water (control)		Ozonated water	
	Biopsy channel	Suction channel	Biopsy channel	Suction channel
Olympus GIF Q10				
Pre-treatment	8.58	8.41	8.43	8.54
Post-treatment				
Cycle 1	4.74	3.63	5.95	6.33
Cycle 2	3.70	4.46	6.04	6.39
Cycle 3	4.17	4.45	6.17	6.39
Mean log₁₀ RF	4.20	4.09	6.05	6.33
Fujinon Colonoscope				
Pre-treatment	8.59	8.69	8.59	8.69
Post-treatment				
Cycle 1	5.48	5.28	5.75	5.99
Cycle 2	5.55	5.46	6.44	6.61
Mean log₁₀ RF	5.52	5.37	6.10	6.30

CLAIMS

1. A method of disinfecting medical theatre
care equipment comprising the steps of causing
5 ozonated water to flow over the surfaces of the
equipment at a predetermined concentration and flow
rate for a predetermined time and monitoring the
concentration of ozone in the water leaving the
equipment and terminating the flow when the
10 concentration of ozone leaving the equipment is
substantially the same as that being delivered to the
equipment.

2. A method as claimed in claim 1, wherein the
15 equipment is subjected to a manual washing process
prior to disinfection by ozonated water.

3. A method as claimed in claim 1 or claim 2,
wherein the ozonated water has a concentration of at
20 least 5 ppm and not more than 15 ppm.

4. A method as claimed in claim 3, wherein the
ozonated water has a concentration of 15ppm.

5. A method as claimed in claim 3 or claim 4,
25 wherein the flow rate of ozonated water over the
surfaces of the equipment is approximately 2.2 litres
per minute.

6. A method as claimed in any of the preceding
30 claims, wherein the equipment has an internal channel
or channels, wherein ozonated water is delivered over
the outer surfaces of the equipment and through the
internal channels of the equipment.

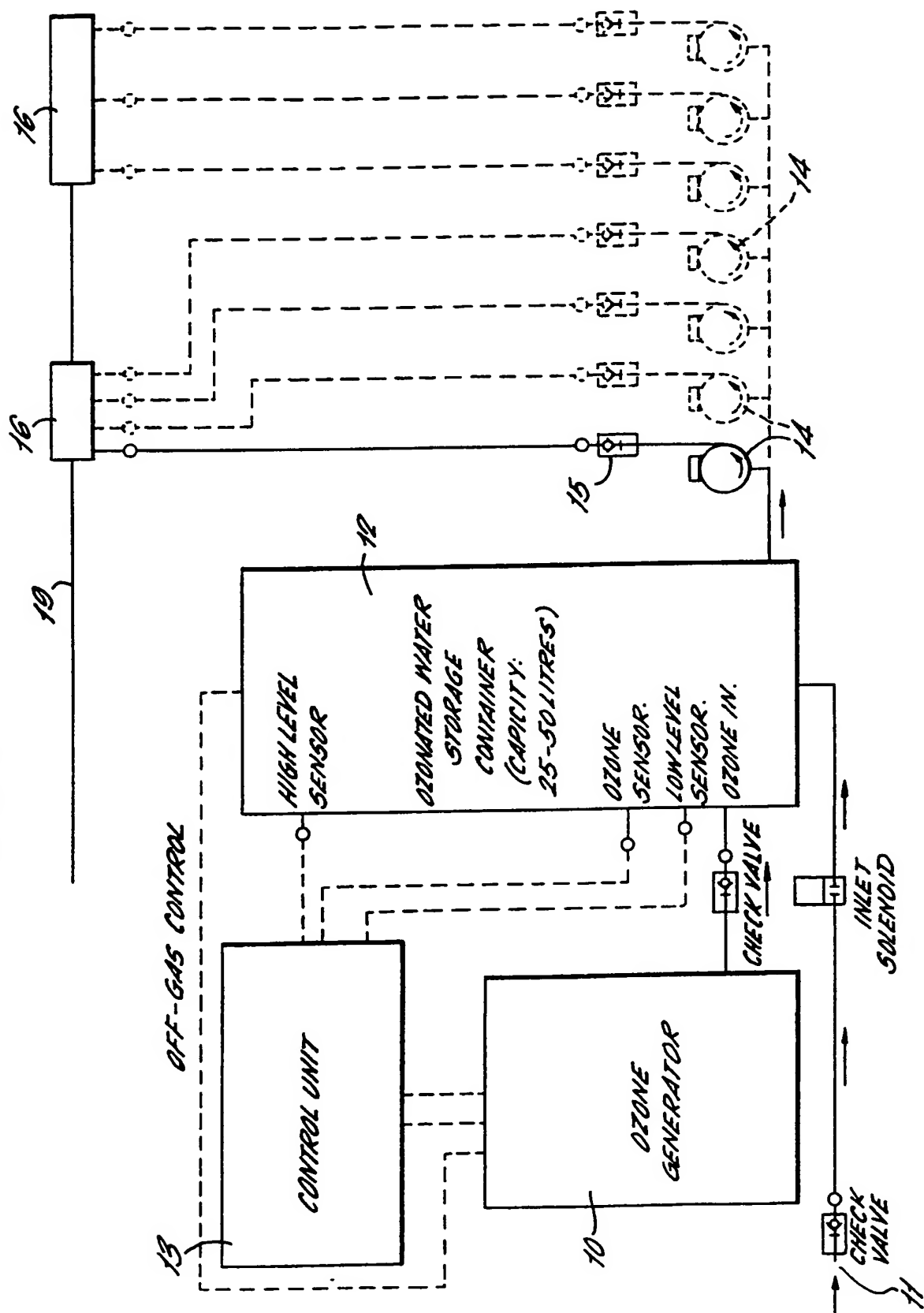
35 7. A method as claimed in any of the proceeding
claims when the equipment is an endoscope having one

or more internal channels through which said ozonated water is caused to flow.

- 5 8. A method as claimed in any of the preceding claims, wherein the equipment is subjected to a final rinse in water following said disinfecting process.

1/4

FIG. 1.



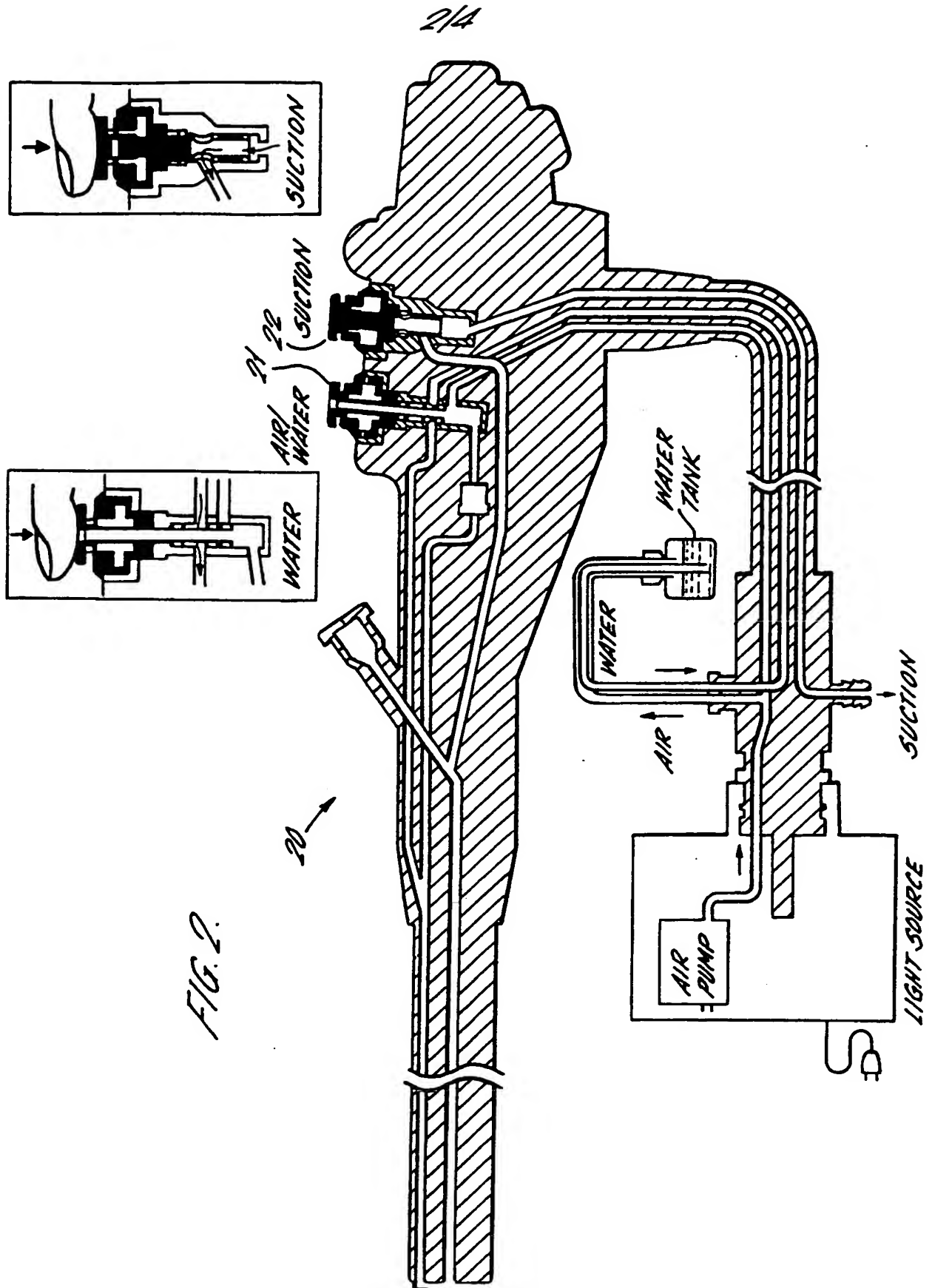
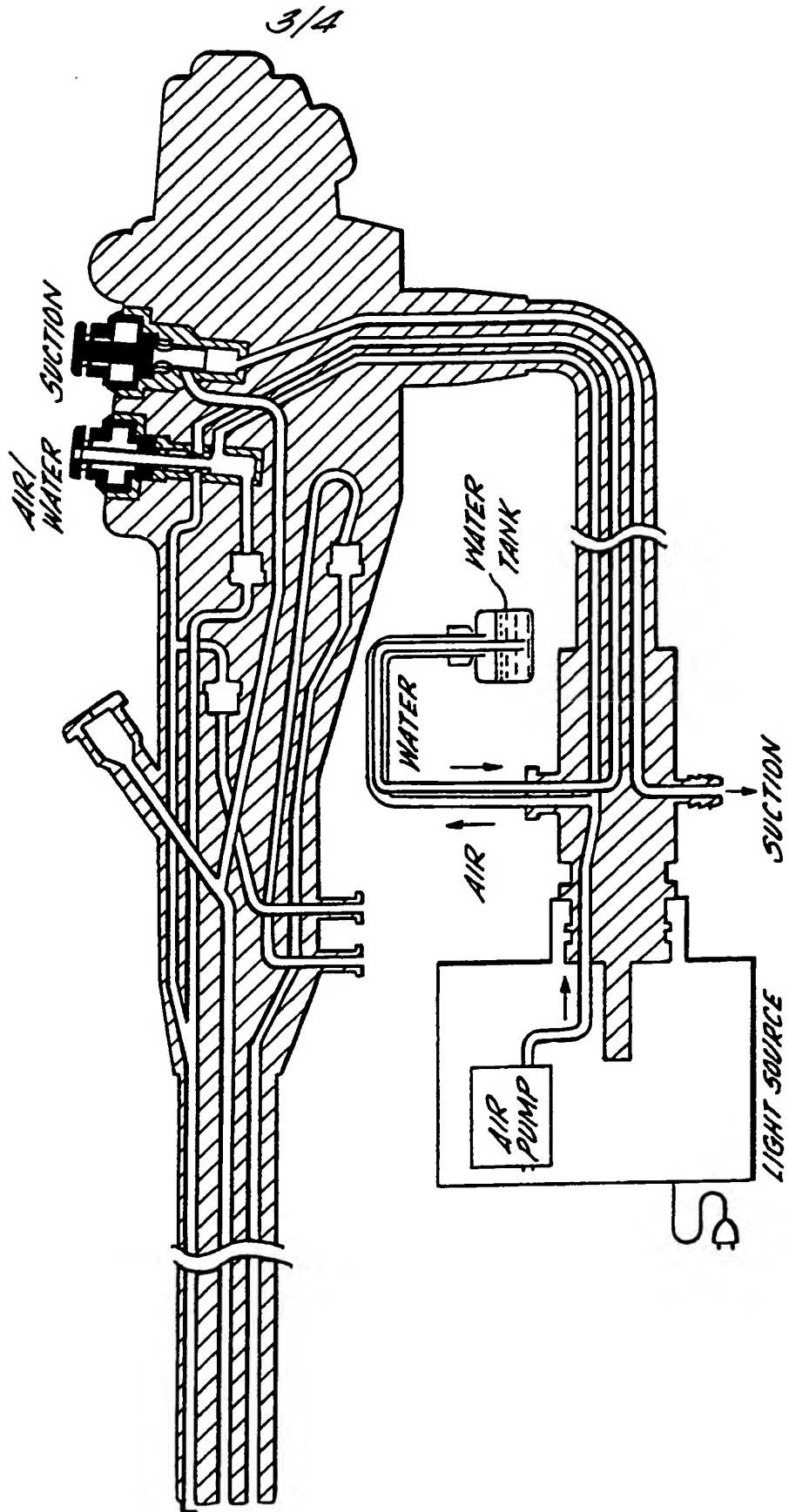
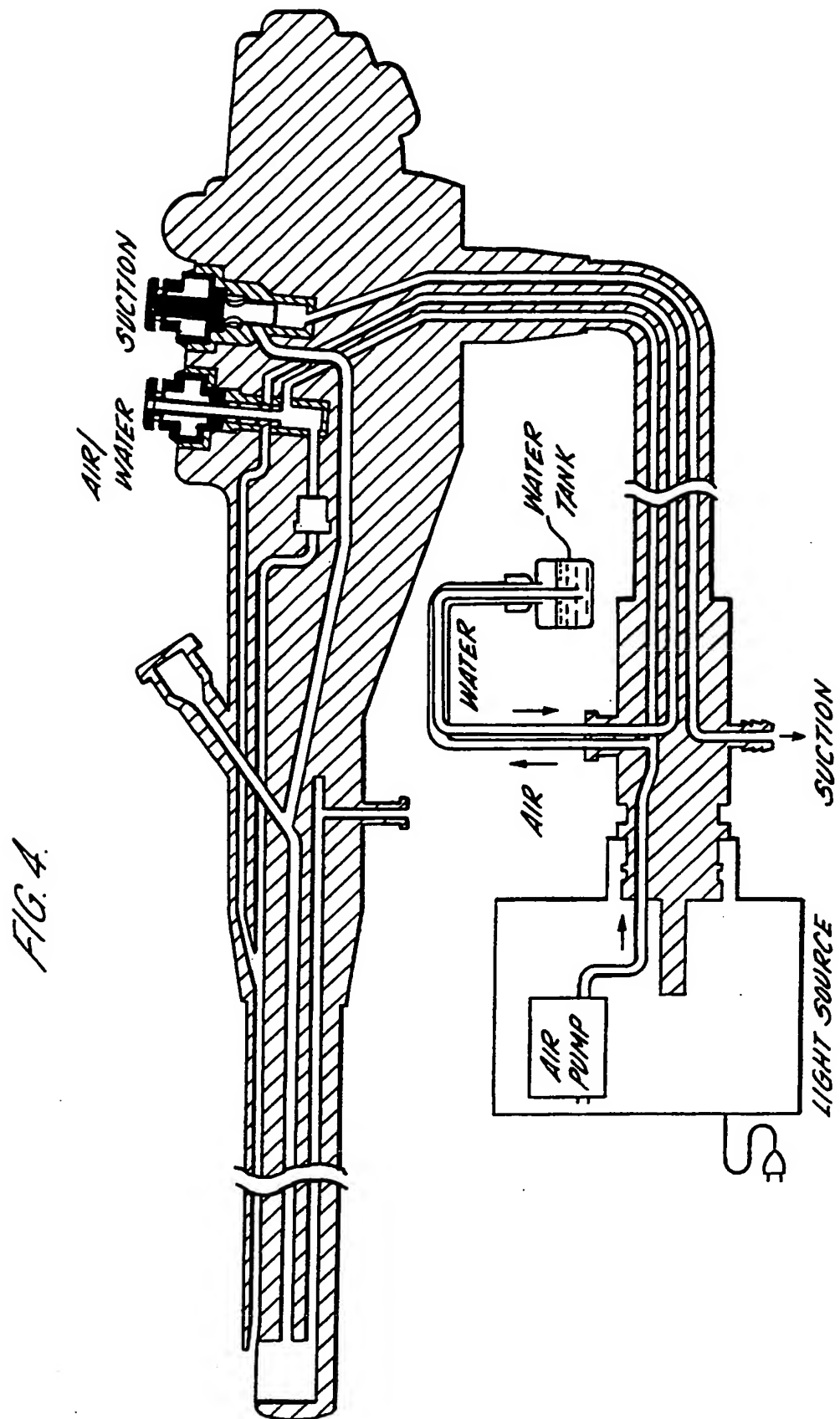


FIG. 3.



4/4



A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L2/20 A61L2/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 443 801 A (LANGFORD TERRENCE R) 22 August 1995 (1995-08-22) claims	1, 2, 6-8
X	US 5 520 893 A (KASTING JR JOHN R ET AL) 28 May 1996 (1996-05-28) claims	1
X	EP 0 773 031 A (CORE CORP) 14 May 1997 (1997-05-14) claims	1
A	US 5 853 014 A (ROSENAUER CHARLES E) 29 December 1998 (1998-12-29) claims; figures	1-8



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

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European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

ESPINOSA, M

INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 97 40860 A (PORTER BROOKS S)</p> <p>6 November 1997 (1997-11-06)</p> <p>claims</p> <p>-----</p>	1-8

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5443801	A	22-08-1995	US 5245845 A	21-09-1993
			US 5184633 A	09-02-1993
			AT 193664 T	15-06-2000
			AU 682870 B	23-10-1997
			AU 6834794 A	12-12-1994
			CA 2162697 A	24-11-1994
			DE 69424867 D	13-07-2000
			DE 69424867 T	15-02-2001
			EP 0700319 A	13-03-1996
			JP 9501845 T	25-02-1997
			WO 9426432 A	24-11-1994
			AU 2781492 A	03-05-1993
			CA 2120628 A	15-04-1993
			EP 0642393 A	15-03-1995
			JP 7500428 T	12-01-1995
			WO 9306948 A	15-04-1993
			US 5207237 A	04-05-1993
US 5520893	A	28-05-1996	NONE	
EP 0773031	A	14-05-1997	JP 9122665 A	13-05-1997
			CA 2189175 A	01-05-1997
US 5853014	A	29-12-1998	US 5641456 A	24-06-1997
			AU 6342698 A	22-09-1998
			WO 9839108 A	11-09-1998
WO 9740860	A	06-11-1997	US 5897832 A	27-04-1999
			AU 2595097 A	19-11-1997
			EP 1061960 A	27-12-2000
			US 6076808 A	20-06-2000